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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,138	11/12/98	BOSCH H	029318/0109

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EXAMINER	
MCQUEENEY,P	
ART UNIT	**PAPER NUMBER**
1615	11

DATE MAILED: 02/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/190,138	BOSCH ET AL.	
	Examiner	Art Unit	
	P. E. McQueeney	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-36,40-45,47-49 and 51-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-36,40-45,47-49 and 51-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Acknowledgement is made of applicants' amendment under 37 CFR 1.111 filed November 27, 2000.

Claim Rejections - 35 USC § 112

2. Claims 11, 23, 35, 40 and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 11, 23, 35, 40 and 42-44 fail to correspond in scope with that which applicant(s) regard as the invention can be found in Paper No. 10 filed November 27, 2000. In that paper at page 17, section III.A., applicant has stated "[t]he liquid dispersion is not limited to water," and this statement indicates that the invention is different from what is defined in the claims because the application as originally filed is directed to water insoluble active ingredients. To support this statement, applicants are directed to page 5, lines 3-4 (attempts to develop respirable aqueous suspensions of poorly soluble drugs); page 5, line 6 (fluorescein and latex particles, representing insoluble drug particles); page 6, line 1 (corticosteroids); page 6, lines 24-25 (the difficulty of formulating dry powder and aqueous aerosols of water-insoluble drugs); page 7, line 5 (the drug is highly water-insoluble); page 7, lines 9-11 (water-insoluble drugs); page 7, lline 27 (aqueous nanoparticulate drug dispersions); page 8, line 11 (aqueous dispersions of a nanoparticulate drug); page 8, line 17 (aqueous dispersion of drug); page 9, line 11 (aqueous dispersion of drug); page 9, line 28 (aqueous dispersions of drug nanoparticles); page 11, Figures (beclomethasone dipropionate, naproxen, polyvinylpyrrolidone); page 12, Figures (triamcinolone acetonide,

budesonide); page 14, line 23 (water-insoluble nanoparticulate drug); page 15, line 17-18 (water-insoluble drug); page 15, lines 25 and 28 (water-insoluble drugs); page 16, line 2 (water-insoluble drugs); page 16, line 15 (aqueous dispersions of nanoparticles); page 18, line 8 (aqueous dispersion of nanoparticulate drug); page 20, lines 22 and 24 (aqueous dispersion of nanoparticles); page 23, lines 11 and 13 (water-insoluble drugs); page 23, line 24 (water-insoluble nanoparticulate drugs). Applicant's argue at page 17 of the amendment filed November 27, 2000 that the paragraph spanning the bottom of page 24 to the top of page 25 should control and that paragraph does not include the phrase water-insoluble. It is the position of the examiner that by the time the person of ordinary skill in the art reaches page 24, sufficient evidence has been presented to show that applicants are disclosing water-insoluble drugs.

3. Claims 65-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65 and 66 recites the limitation "the aerosol composition of claim 42" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 67 and 68 recites the limitation "the aerosol composition of claim 43" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 69 and 70 recites the limitation "the aerosol composition of claim 44" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Applicant is recommended to amend claims 42 and 43 so as to recite an aerosol composition, as opposed to an aerosol formulation, or to amend claims 65-68 to recite an aerosol formulation. Applicant is recommended to amend claims 69 and 70 to recite "the dry powder nanoparticulate drug composition of claim 44."

Claim Rejections - 35 USC § 102

4. Claims 11-14, 16-25, 27-33, 40, 41, 44 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards *et al.* (US 5,985,309).

Applicants' arguments filed November 27, 2000 have been fully considered but they are not persuasive.

In response to applicants' arguments, the recitation "spray-dried powder aerosol" of claim 11, "freeze-dried powder aerosol" of claim 23, "dry powder nanoparticulate drug composition" of claims 40 and 44 have not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Applicants argue that Edwards *et al.* do not teach applicants' claimed drug particle sizes. Applicants' amended claims recite dry powder nanoparticulate drug aerosols in which at least 50% of the drug particles have a geometric particle size of

less than about 1 μm, which form aggregates having a particle size of less than about 100 μm in diameter. It is the position of the examiner that Edwards *et al.* meet this limitation. Applicants are directed to claim 1, for example, which claims particles for drug delivery consisting of a therapeutic agent and a material selected from the group consisting of surfactant and a molecule having a charge opposite to the charge of the therapeutic agent and forming a complex thereto, wherein the particles have ... a mean diameter of between 5 μm and 30 μm (reading on applicants' less than 100 μm limitation) effective to yield an aerodynamic diameter (according to applicants at page 16 of the amendment filed November 17, 2000, this term is equal to the geometric diameter times the square root of the density) of the particles of between approximately one and five microns. Edwards *et al.* do not specifically state that 50% of the particles have a geometric particle size of less than about 1 μm, but Edwards *et al.* do state that their aerodynamic diameter is approximately 1 to 5 μm and their tap density is less than 0.4 g/cm^3. Per applicants' formula, Edwards *et al.* claim a geometric diameter of 1 to 5 μm/(0.4 g/cm^3)^{½}, or 1.6 μm to 8 μm. Furthermore, Edwards *et al.* claim an aerodynamic particle size of *approximately* 1 to 5 μm. So the geometric diameter would be approximately 1.6 μm. This limitation reads on applicants' geometric particle size of less than about 1 μm.

This rejection is maintained and applied to newly added claims 59-62, 69-71, 73, 75, 77, 79, 81, 90, 92-95, 111 and 113-116.

Claim Rejections - 35 USC § 103

5. Claims 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei *et al.* (WO 95/27475) and Liversidge *et al.* (EP 0 499 299 A2).

Applicants argue that Adjei *et al.* do not disclose applicants' claimed particle size. Applicants also focus on different aspects of Adjei *et al.* than examiner had referenced. Applicants are directed to page 1, lines 26-31. Applicants claim a method. Adjei *et al.* disclose this method at page 1, lines 26-31. Adjei *et al.* do not specifically state applicants' claimed particle size. However, Adjei *et al.* teach the same method. Adjei *et al.* further teach that this method is performed until the desired particle size is obtained. As Adjei *et al.* perform applicants' instant method, Adjei *et al.* meet the limitations of applicants' claim 42.

Applicants argue that Liversidge *et al.* do not teach or suggest aerosol dosage forms comprising a nanoparticulate drug. Examiner did not rely upon Liversidge *et al.* for this proposition. Examiner relied upon Liversidge *et al.* at page 5, lines 46-51 that teaches that pressures are altered in milling processes by one of ordinary skill in the art to affect the desired outcome. Again, the dry powder nanoparticulate drug composition is a limitation in the preamble of claim 42 (see above regarding preambles).

This rejection is maintained and applied to newly added claims 67-70.

6. Claims 97-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei *et al.* and Liversidge *et al.*, as discussed above.

Adjei *et al.* and Liversidge *et al.* are relied upon to show the teaching of applicants' method claims 43 and 44 is well known in the art. Newly added claims 104-117 depend from these method claims. Claims 97 and 104 provide a laundry list of potential drug selections. Adjei *et al.* only teach solid therapeutic agents (page 1, line 27). Liversidge *et al.* disclose at page 3, line 30 through page 4, line 12 that their invention can be practiced with a wide variety of drug substances. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to utilize any of the drug substances listed at page 3, line 30 through page 4, line 12 of Liversidge in the teachings of Adjei *et al.* and Liversidge *et al.* in order form particles of solid therapeutic agents of reduced size. The expected result would be nanoparticulate drug suspensions.

7. Claims 11-34, 40, 41, 44, 45, 47, 48 and 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards *et al.*, as discussed above.

Applicants argue that the particle size of the active substance is a critical limitation of their invention. Applicants argue that nanoparticulate drug particles enable dry powder aerosols for deep lung delivery. However, Edwards *et al.* teach drug delivery to the pulmonary system (i.e., deep lung delivery). Applicants argue at page 23, line 26 through page 24, line 6 of the application that when micronized drug is incorporated into larger droplet sizes (which Edwards *et al.* do not have, they have smaller droplet sizes), not all droplets of the aerosol formulation include drug and therefore do not exhibit the rapid and efficient drug delivery enabled by the

nanoparticulate aerosol formulations of applicants' invention. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

This rejection is maintained and applied to newly added claims 59-62, 69-82, 90-96 and 111-117.

8. Claims 11-36, 40, 41, 44, 45, 47-49 and 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards *et al.*, as discussed above, in combination with Smith *et al.* (US 5,785,049).

Applicants argue that Edwards *et al.* do not disclose the use of nanoparticulate drugs in dry powder aerosol compositions. Again, applicants are arguing a limitation from the preamble.

This rejection is maintained and applied to claims 59-64, 69-96 and 111-117.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. E. McQueeney whose telephone number is 703-306-5827. The examiner can normally be reached on M, T, H, F 7:45 AM to 6:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-3592 for regular communications and 703-308-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

THURMAN K. PAGE
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